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49. The computer program product of claim 40 wherein said plurality of cells are from a plurality of different cell lines.

50. The computer program product of claim 49, wherein a morphological value is captured for each of said plurality of different cell lines; wherein a degree of presence is assigned and stored for each of said morphological values; and wherein said code for producing a statistical profile of said manipulated cells comprises code for comparing or clustering the degrees of presence for each of said morphological values for each of said plurality of different cell lines.

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51. The computer program product of claim 40 wherein the cells are NCI-H460, A549, MDA-MD-231, MCF-7, SK-OV-3, OVCA-3, A498, U-2 OS, or HeLa cells.

REMARKS

Applicants respectfully request reconsideration of the rejections set forth in the Office Action mailed on October 23, 2001. Claims 1-39 and 46-48 have been withdrawn from consideration and have been cancelled herein without prejudice. Claim 44 has also been cancelled. Claims 49-51 have been added. Thus, Claims 40-43, 45, and 49-51 are pending. Claims 40-45 were rejected.

This amendment is to expedite prosecution and should not be construed as acquiescence in any ground of rejection. Applicants reserve the right to prosecute the originally filed claims in the future. A clean version of the amended claims with instructions for entry pursuant to 37 C.F.R. §1.121(c)(1)(i) is included above. A marked-up version of the amended claims pursuant to 37 C.F.R. §1.121(c)(1)(ii) is attached. The comments in the Office action are now addressed in turn.

Informalities

The Examiner has noted embedded hyperlinks and blanks in the Specification; Applicants believe that the above amendments to the specification appropriately correct these informalities.

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Rejections under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 40-45 under 35 U.S.C. § 112, second paragraph. More specifically, the Examiner has expressed concerns regarding whether the action of capturing the morphological value occurs during the action of manipulation or after the cell has been manipulated. In addition, the Examiner has indicated that there is a lack of clarity in determining a relationship between two components of a cell. Finally, it is argued that Claim 40 is vague and indefinite in the manner that is the body of the claim does not set forth that which the preamble sets out to perform. The claims have been amended to address this rejection. Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. §102

Claims 40-45 have been rejected under 35 U.S.C. §102(b) as being anticipated by Giuliano et al. (1997) J. of Biomol. Screening 2:249-259 ("Giuliano"). The rejection is respectfully traversed as applied to the amended claims.

As repeatedly indicated by the courts, anticipation requires that all of the elements and limitations of the claim be found within a single prior art reference. There must be no difference between the claimed invention and the disclosure provided by the reference, as viewed by a person of ordinary skill in the field of the invention. (*Scripps Clinic & Research Fdn. v. Genentech, Inc.*, 927 F.2d 1565, 1576 [Fed. Cir. 1991]). Furthermore, "[t]o establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. (*In re Royka*, 490 F.2d 981, 180 USPQ 580 [CCPA 1974]). Applicants submit that Giuliano does not teach every element of the claims; therefore, that the invention, as claimed herein, is not anticipated by Giuliano.

The present invention, as claimed herein, relates to a computer program product for mapping a manipulation of cells based upon a statistical analysis of a morphological value. More specifically, *a plurality of cells from one or more cell lines* are manipulated with one or more factors. The effects of such manipulations on at least *two* components of the cells are quantified and/or qualified through the use of morphological values. The values are captured and assigned a degree of presence. The morphological values and their associated degree of presence will change according to the nature of the manipulation. Such changes are sufficiently unique to permit a correlation to be drawn between similar morphological values when statistically analyzed.

Giuliano is said to describe "high-content" screening that provides measurements of nuclear size and shape changes, nuclear DNA content, mitochondrial potential, and actin-

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cytoskeletal rearrangements of a plurality of cells resulting from manipulating of cells. Giuliano is also said to describe sources of manipulation including thermal, biological and temporal. Figure 8 is said to demonstrate the assignment and storage of morphological values in the captured images of morphometric data *from a single cell*.

Significantly, Giuliano does not teach or suggest any methods for comparing data from one cell with that from another cell (from the same or from a different experiment). Rather, as exemplified in Figure 8, Giuliano captures images of data from a *single* cell. Giuliano does not teach or suggest the use of statistical analysis techniques employing techniques such as multidimensional representations, frequency-based representations, multidimensional cluster analysis techniques, and the like. Giuliano does not teach or suggest any methods for creating "fingerprints" that quantify and/or qualify the effects of a manipulation on a cell line or methods for comparing one fingerprint to another.

Giuliano does, however, suggest that a bioinformatics application involving the systematic development and application of techniques for managing and analyzing data contained in databases, modeling, and database search regarding multidimensional cellular information is "*daunting*" because of the scale of the multidimensional information that interconnects with chemical and molecular activities within the cell. See, Giuliano at page 258. Although Giuliano remarks that a database has been designed to capture this information, the reference does not teach or suggest any specific information regarding the database or the methods of analysis or search that could be used with it.

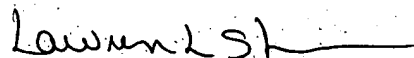
As the elements of Giuliano are *not* the same as those presently claimed, Applicants submit that Giuliano does not anticipate the pending claims and respectfully request that this rejection be withdrawn.

Applicants believe that the claims are allowable and respectfully request a Notice of Allowance for this application from the Examiner. Should the Examiner believe that a telephone

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conference would expedite the prosecution of this application, the undersigned can be reached at the telephone number set out below.

Respectfully submitted,
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MARKED UP VERSION OF AMENDED CLAIMS

40. (Amended) A computer program product ~~[of]~~ for mapping a plurality ~~[manipulation]~~ of cells after applying a manipulation to said plurality of cells, based upon a statistical analysis of a morphological value, said computer program product comprising:

- code for capturing ~~[a]~~ the morphological value from said plurality of manipulated cells ~~[said cells being manipulated]~~;
- code for assigning a degree of presence of said morphological value; [and]
- code for storing said [morphological value and said] degree of presence;
- code for producing a statistical profile of said manipulated cells from said degree of presence; and
- code for mapping said plurality of manipulated cells based upon said statistical profile,

wherein

said morphological value is derived from a first component of a cell and a second component of said cell and wherein said morphological value is one or any combination of a cell count, an area, a perimeter, a length, a breadth, a fiber length, a fiber breadth, a shape factor, an elliptical form factor, an inner radius, an outer radius, a mean radius, an equivalent radius, an equivalent sphere volume, an equivalent prolate volume, an equivalent oblate volume, an equivalent sphere surface area, an average gray value, a total gray value, or an optical density

[said code for capturing said morphometric value from said plurality of cells comprises code for determining a relationship between said first component and said second component]; and

a computer readable storage medium for holding the codes.

45. (Amended) The computer program product of claim 40 wherein said degree of presence is a multiple of a quantized value.

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MARKED UP VERSION OF AMENDED SPECIFICATION

At page 1, please **replace** the section entitled "CROSS-REFERENCES TO RELATED APPLICATIONS" with the following:

The following commonly-owned co-pending applications, including this one, are being filed concurrently and the others are hereby incorporated by reference in their entirety for all purposes:

1. U.S. Patent Application Serial No. [] **09/310,879**, James H. Sabry, et. al., titled, "A DATABASE METHOD FOR PREDICTIVE CELLULAR BIOINFORMATICS," [(Attorney Docket Number 19681-000100US)];
2. U.S. Patent Application Serial No. [] **09/311,890**, James H. Sabry, et. al., titled, "A DATABASE SYSTEM FOR PREDICTIVE CELLULAR BIOINFORMATICS," [(Attorney Docket Number 19681-000200US)];
3. U.S. Patent Application Serial No. [] **60/134,104**, Cynthia L. Adams, et. al., titled, "A DATABASE SYSTEM AND USER INTERFACE FOR PREDICTIVE CELLULAR BIOINFORMATICS," [(Attorney Docket Number 19681-000300US)]; and
4. U.S. Patent Application Serial No. [] **09/311,996**, Eugeni A. Vaisberg, et. al., titled, "A DATABASE SYSTEM INCLUDING COMPUTER CODE FOR PREDICTIVE CELLULAR BIOINFORMATICS," [(Attorney Docket Number 19681-000400US)].

At page 7, please **replace** the paragraph beginning at line 27 with the following **amended** paragraph:

Although the above has been described generally in terms of specific hardware, it would be readily apparent to one of ordinary skill in the art that many system types, configurations, and combinations of the above devices are suitable for use in light of the present disclosure. Of course, the type of system elements used depend highly upon the application. Other examples of systems can be found in co-pending application U.S. Application No. [] **09/311,890** [(Attorney Docket No. 19681-000200)], which has been noted above.

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At page 15, please replace the paragraph beginning at line 29 with the following amended paragraph:

Select embodiments comprising such approaches enable the use of a broad array of sophisticated algorithms to compare, analyze, and cluster gene and protein sequences. Many programs performing this task are known to those of ordinary skill in the art[, such as for example, <http://evolution.genetics.washington.edu/phylip.html>, and <http://evolution.genetics.washington.edu/software.html>].

At page 45, line 26, please replace the paragraph with the following amended paragraph:

Resulting sequences were clustered using an AlignX module commercial software package Vector NTI[(<http://informaxinc.com>)], which uses a Neighbor Joining algorithm for sequence clustering.

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